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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Megan Anne Diehl et al.:

Application No.: 10/665,343

Group No.: 1612

Filed: September 18, 2003

Examiner: Sabiha Naim Qazi

For: SYNERGISTIC MICROBICIDAL COMBINATIONS

MAIL STOP APPEAL BRIEF - PATENTS

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

**APPEAL BRIEF**

This is an appeal from the rejection dated October 23, 2009 finally rejecting claims 1, 3 and 7-15. The rejected claims are set out in Appendix J. Appellants filed a Notice of Appeal pursuant to 37 C.F.R. § 1.191 on January 14, 2010.

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**(C) Real Party In Interest**

The owner of the present application and the invention contained therein is  
ROHM AND HAAS COMPANY.

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**(D) Related Appeals, Interferences or Judicial Proceedings**

No appeals, interferences or judicial proceedings are known to Appellants, the Appellants' legal representative, or the assignee which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

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**(E) Status Of Claims**

The status of the claims is as follows:

Claims pending: 1, 3 and 7-15

Allowed claims: none

Claims objected to: none

Claims canceled: 2 and 4-6

Claims rejected: 1, 3 and 7-15

Claims on appeal: 1, 3 and 7-15

Claims withdrawn from consideration by the Examiner: none.

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**(F) Status Of Amendments**

Appellants have not filed an amendment after final rejection in the present application.

**(G) Summary of Claimed Subject Matter**

**Claim 1:** The present invention provides a microbicidal composition comprising a synergistic mixture, the first component of which is 2-methyl-3-isothiazolone, and the second component of which is one or more commercial microbicides selected from the group consisting of benzoic acid, sorbic acid, 1,2-dibromo-2,4-dicyanobutane, 1,3 dimethylol-5,5-dimethylhydantoin, phenoxyethanol, zinc pyrithione and climbazole [page 2, lines 7-12]; wherein a ratio of 2-methyl-3-isothiazolone to benzoic acid is from 1/0.13 to 1/8 or from 1/20 to 1/67 [page 9, lines 16-18; page 12, Table 1, data for *C. albicans*, *P. aeruginosa*], a ratio of 2-methyl-3-isothiazolone to sorbic acid is from 1/4 to 1/20 [page 9, lines 21-23; page 15, Table 3, data for *S. aureus*], a ratio of 2-methyl-3-isothiazolone to 1,2-dibromo-2,4-dicyanobutane is from 1/10 to 1/20 [page 16, Table 4, data for *P. aeruginosa*], a ratio of 2-methyl-3-isothiazolone to 1,3 dimethylol-5,5-dimethylhydantoin is from 1/11 to 1/20 [page 17, Table 5, data for *P. aeruginosa*], a ratio of 2-methyl-3-isothiazolone to phenoxyethanol is from 1/30 to 1/80 or from 1/107 to 1/133 [pages 18-19, Table 6, data for *P. aeruginosa*], a ratio of 2-methyl-3-isothiazolone to zinc pyrithione is from 1/0.16 to 1/2.7 [pages 19-20, Table 7, data for *A. niger*, *P. aeruginosa*], and a ratio of 2-methyl-3-isothiazolone to climbazole is from 1/0.6 to 1/1.3 [page 21, Table 8, data for *C. albicans*]; and wherein the composition is substantially free of halogenated 3 isothiazolone [page 2, lines 13-14].

**Claim 9:** The present invention further provides a microbicidal composition comprising a synergistic mixture, the first component of which is 2-methyl-3-isothiazolone, and the second component of which is one or more commercial microbicides selected from the group consisting of citric acid and benzyl alcohol; wherein the ratio of the first component to the second component is from 1/8 to 1/24 when the second component is citric acid; wherein the ratio of the first component to the second component is from 1/0.13 to 1/32 or from 1/80 to 1/600 when the second component is benzyl alcohol; and wherein the composition is substantially free of halogenated 3

isothiazolone [page 2, lines 15-23; pages 22-23, Table 9, overlapping ranges for all four organisms].

**Claim 10:** The present invention further provides a method of inhibiting the growth of microorganisms in a locus comprising introducing to, at or on, the locus a microorganism inhibiting amount of a synergistic mixture [page 2, lines 24-26] the first component of which is 2-methyl-3-isothiazolone, and the second component of which is one or more commercial microbicides selected from the group consisting of benzoic acid, sorbic acid, 1,2-dibromo-2,4-dicyanobutane, 1,3 dimethylol-5,5-dimethylhydantoin, phenoxyethanol, zinc pyrithione and climbazole [page 2, lines 7-12]; wherein a ratio of 2-methyl-3-isothiazolone to benzoic acid is from 1/0.13 to 1/8 or from 1/20 to 1/67 [page 9, lines 16-18; page 12, Table 1, data for *C. albicans*, *P. aeruginosa*], a ratio of 2-methyl-3-isothiazolone to sorbic acid is from 1/4 to 1/20 [page 9, lines 21-23; page 15, Table 3, data for *S. aureus*], a ratio of 2-methyl-3-isothiazolone to 1,2-dibromo-2,4-dicyanobutane is from 1/10 to 1/20 [page 16, Table 4, data for *P. aeruginosa*], a ratio of 2-methyl-3-isothiazolone to 1,3 dimethylol-5,5-dimethylhydantoin is from 1/11 to 1/20 [page 17, Table 5, data for *P. aeruginosa*], a ratio of 2-methyl-3-isothiazolone to phenoxyethanol is from 1/30 to 1/80 or from 1/107 to 1/133 [pages 18-19, Table 6, data for *P. aeruginosa*], a ratio of 2-methyl-3-isothiazolone to zinc pyrithione is from 1/0.16 to 1/2.7 [pages 19-20, Table 7, data for *A. niger*, *P. aeruginosa*], and a ratio of 2-methyl-3-isothiazolone to climbazole is from 1/0.6 to 1/1.3 [page 21, Table 8, data for *C. albicans*]; and wherein the composition is substantially free of halogenated 3 isothiazolone [page 2, lines 6-7]; and wherein the amount of synergistic mixture is from 0.1 to 10,000 parts per million active ingredient [page 2, lines 18-19].



**(H) Grounds of Rejection to be Reviewed on Appeal**

Claims 1, 3 and 7-15 stand rejected under 35 U.S.C. § 103(a) as unpatentable over U.S. 6,361,788 to Antoni-Zimmerman et al. ("Antoni-Zimmerman").

(I) Argument

Regarding whether or not claims 1, 3 and 7-15 are unpatentable over U.S. 6,361,788 to Antoni-Zimmerman et al. ("Antoni-Zimmerman"):

A finding of obviousness may be rebutted by demonstrating unexpected results relative to the prior art disclosure. *See In re Woodruff*, 919 F.2d 1575, 1578 (Fed. Cir. 1990); M.P.E.P. § 2144.05(III). Appellants have demonstrated (see specification, pages 12-23) that their claimed biocide combinations display synergistic activity (synergy index  $< 1$ ) within the claimed ranges of biocide ratios. The Declarations of Eileen F. Warwick, submitted January 23, 2009 and June 17, 2009, are of record in this case. The declarant states that the existence of synergy between any pair of biocides, and also the range of biocide ratios over which it occurs, could not have been predicted. The cited reference does nothing to lead one to expect Appellants' claimed results. Antoni-Zimmerman et al. discloses or suggests synergistic interactions only between 2-methyl-3-isothiazolone ("MI") and 1,2-benzisothiazolone ("BIT"), and between the MI/BIT combination and a small list of other biocides. While a long list of additional biocides is provided, some of which are combined with MI in the present claims, there is no suggestion in the reference that any of the biocide combinations claimed by Appellant would produce a synergistic result. Declarant's statement that any particular synergistic interaction could not have been expected, coupled with the lack of any suggestion in the reference or any other evidence of record that Appellants' results would have been expected, make it clear that the synergy discovered by Appellants could not be obvious over the disclosure of Antoni-Zimmerman.

The Office appears to question the validity of declarant's statement that synergy in the claimed ranges could not have been predicted, and in so doing gives more weight to its own evaluation than to that of an expert. The statement of an expert "in this field is entitled to more weight than that of a layman," and by not accepting declarant's statements and not providing any other evidence suggesting predictability of the results, the Office has "erroneously substituted its judgment for that of an established expert in the art." *In re Zeidler*, 682 F.2d 961, 966-7 (C.C.P.A. 1982); see also, *In re Neave*, 370 F.2d 961 (C.C.P.A. 1967), *Ex parte Ridyard*, 2001 Pat. App. LEXIS 132 (B.P.A.I. 2001).

The final Office Action argues that efforts to find synergistic combinations are merely “routine experimentation” (final Office Action, page 11). This argument typically is used in establishing a *prima facie* case of obviousness. See, e.g., *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775 (Fed. Cir. 1985); *In re Aller*, 220 F.2d 454 (C.C.P.A. 1955); M.P.E.P. § 2144.05. Appellants do not see its relevance to their rebuttal argument that they have obtained unexpected results. The declarations of record attest to the fact that one skilled in the art would not have expected the claimed results, and there is no contrary evidence of record that indicates otherwise. Moreover, the testing required to find synergistic combinations and their effective ranges is much more extensive than the “mere optimization” described in *Titanium Metals Corp.* and *In re Aller*. In those cases, the optimization consisted only of making small variations in percent composition of an alloy, and in two reaction parameters, respectively.

Antoni-Zimmerman provides a long list of biocides (column 3, line 5 to column 4, line 7), not coupled with any suggestion regarding synergy, and further disclosure that one would observe synergy between the MI/BIT combination and a much shorter list of biocides (column 4, lines 42-45). However, none of the biocides on the shorter list is within the scope of the present claims. Based on these disclosures, one would need to: (1) test possible combinations of MI<sup>1</sup> and biocides from the longer list to determine if synergy exists; and (2) conduct extensive testing to determine the range of biocide ratios in each combination over which synergy actually exists. In assessing a *prima facie* case of obviousness, the Court of Appeals for the Federal Circuit has required that “to have a reasonable expectation of success, one must be motivated to do more than merely to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result.” *Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1165 (Fed. Cir. 2006) (citing *In re O’Farrell*, 853 F.2d 894, 903-4 (Fed. Cir. 1988)). In the present case, as described above, one would need to do extensive testing to discover synergistic combinations and their synergistic ranges, without any reasonable expectation of success

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<sup>1</sup> Appellants recognize that the claims are in “comprising” form and also would encompass combinations of MI/BIT and a third biocide, but synergy in these combinations would have been as unexpected as that between MI and a third biocide for the reasons stated in this Appeal Brief.

with any particular combination, and therefore any synergistic biocide combinations and ranges discovered by such testing could not have been expected. Every invention requires testing, so to say that any testing that might lead to discovery of unexpected, previously unknown effects is "routine experimentation," and that the results of such testing would have been expected, amounts to saying that nothing is patentable.

The final Office Action appears to rely on *Ex parte Quadranti*, 1992 Pat. App. LEXIS 26 (B.P.A.I. 1992) to argue that synergy is not unexpected. However, there are important differences between the factual situation in *Quadranti* and that in the present application. In *Quadranti*, the Board objected to the Colby equation used to demonstrate synergy, stating that it was not considered valid by workers in the field. *Id.* at \*2-\*3. Here, Appellants are relying on the Synergy Index (SI) described by Kull, F.C.; Eisman, P.C.; Sylwestrowicz, H.D. and Mayer, R.L., in *Applied Microbiology* 9:538-541 (1961), an accepted method for determining synergy, as stated on page 9 of the present application. In *Quadranti*, the Board also stated that "[t]he Colby equation inherently results in an expectation of a less than additive effect for any combination." *Quadranti* at \*2. This is not true of the method used by Appellants, as evidenced by ratios at which additive behavior or even antagonism is observed (specification, pages 10-21).

The Board in *Quadranti* also objected to the fact that the data presented did not show very good effectiveness. *Id.* at \*5. In the present application, the SI values are calculated from minimum inhibitory concentration (MIC) of each component, which "is the concentration tested under a specific set of conditions that prevents the growth of added microorganisms" (see specification, page 9, lines 19-20). Therefore, each SI represents a combination of biocides that actually prevents growth of microorganisms.

Appellants have made these arguments with regard to *Ex parte Quadranti* in previous responses which are of record, and yet none of the Office Actions specifically addresses these arguments. The final Office Action contains only lengthy quotes from the case with no analysis to support the Office Action's apparent assertion that *Quadranti* supports the proposition that synergy should have been expected in the present application. Likewise, the final Office Action does not address the statements made by declarant regarding the unexpectedness of synergistic interactions. The Office Action

merely reiterates earlier statements that MI displays synergy with some particular biocides, as shown in the reference, but ignores declarant's statement that the claimed synergistic interactions between MI and other biocides could not have been predicted. "Office personnel should avoid giving evidence no weight." M.P.E.P. § 2145; see also *In re Zeidler* and other cases cited above.

The final Office Action also cites *In re Kollman* (595 F.2d 48 (C.C.P.A. 1979)), a case dealing with synergy between herbicides, and characterizes the court's holding as: "the limited number of species exemplified did not provide an adequate basis for concluding that similar results would have been obtained for the other diphenyl ether herbicides within the scope of the generic claims" (final Office Action, page 8). In so stating, the Office appears to admit that one could not predict the existence of synergy for combinations of compounds which have not been tested. That being the case, any synergistic interactions one might observe could not have been expected. In the present case, Appellants are claiming only combinations for which synergy has been demonstrated, and only over the ranges for which synergy actually was observed.

The final Office Action also includes quotations attributed to other cases, including *KSR* and *Brenner*, but without showing how these cases relate to the present application. The quotes attributed to *Brenner* are particularly puzzling. They include the statement that "patent protection is granted in return for an enabling disclosure of an invention, not for vague limitations of general ideas that may or may not be workable" (final Office Action, page 15). Appellants have claimed a specific invention whose enabling disclosure has not been questioned and they have shown that the claimed combinations in fact inhibit growth of at least one microorganism better than the individual biocides. Therefore, there is nothing "vague" or "general" or "not ... workable" about the present claims or specification.

As for *KSR*, the Supreme Court stated that the "combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR Int'l v. Teleflex*, 550 U.S. 398, 416 (2007) (emphasis added). In the present application, known biocides were combined, but the combination did not yield predictable results, as attested to in the declarations of record in this case.

Accordingly, *KSR* cannot be relied on with regard to the present application. The Federal Circuit rejected the application of *KSR* in cases with a showing of unpredictable results in *Sanofi-Synthelabo v. Apotex*, 550 F.3d 1075 (Fed. Cir. 2008). In that case, the patentee isolated one enantiomer of a known racemic drug and obtained an unpredictable result. The Federal Circuit quoted the passage cited above from *KSR* and held that “the result of this separation of enantiomers was unpredictable” and that accordingly “the principles of *KSR* do not affect the conclusion herein.” 550 F.3d at 1090. In the present application, the biocide combinations also did not yield predictable results. The existence of synergy between any pair of biocides cannot be predicted, and the ranges over which synergy was observed also were not predictable, as stated in the declarations submitted previously. The result in *Sanofi-Synthelabo* is equally applicable to this case and requires that *KSR* does not apply when unpredictable results are obtained.

#### CONCLUSION

Based on the foregoing, Appellants respectfully submit that the pending claims are currently in condition for allowance. Appellants respectfully request the Board to pass the pending claims to allowance. Enclosed herewith, Appellants have filed a Certificate of Mailing to establish the timely filing of this Appeal Brief. The Commissioner is hereby authorized to charge any additional fee which may be required, or to credit any overpayments to Deposit Account 18-1850.

Respectfully submitted,



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January 26, 2010

(J) Claims Appendix

1. A microbicidal composition comprising a synergistic mixture, the first component of which is 2-methyl-3-isothiazolone, and the second component of which is one or more commercial microbicides selected from the group consisting of benzoic acid, sorbic acid, 1,2-dibromo-2,4-dicyanobutane, 1,3 dimethylol-5,5-dimethylhydantoin, phenoxyethanol, zinc pyrithione and climbazole; wherein a ratio of 2-methyl-3-isothiazolone to benzoic acid is from 1/0.13 to 1/8 or from 1/20 to 1/67, a ratio of 2-methyl-3-isothiazolone to sorbic acid is from 1/4 to 1/20, a ratio of 2-methyl-3-isothiazolone to 1,2-dibromo-2,4-dicyanobutane is from 1/10 to 1/20, a ratio of 2-methyl-3-isothiazolone to 1,3 dimethylol-5,5-dimethylhydantoin is from 1/11 to 1/20, a ratio of 2-methyl-3-isothiazolone to phenoxyethanol is from 1/30 to 1/80 or from 1/107 to 1/133, a ratio of 2-methyl-3-isothiazolone to zinc pyrithione is from 1/0.16 to 1/2.7, and a ratio of 2-methyl-3-isothiazolone to climbazole is from 1/0.6 to 1/1.3; and wherein the composition is substantially free of halogenated 3 isothiazolone.

3. The composition of claim 1 wherein the second component comprises sorbic acid and the ratio of 2-methyl-3-isothiazolone to sorbic acid is from 1/4 to 1/20.

7. The composition of claim 1 wherein the second component comprises zinc pyrithione and the ratio of 2-methyl-3-isothiazolone to zinc pyrithione is from 1/0.16 to 1/2.7.

8. The composition of claim 1 wherein the second component comprises climbazole and the ratio of 2-methyl-3-isothiazolone to climbazole is from 1/0.6 to 1/1.3.

9. A microbicidal composition comprising a synergistic mixture, the first component of which is 2-methyl-3-isothiazolone, and the second component of which is

one or more commercial microbicides selected from the group consisting of citric acid and benzyl alcohol; wherein the ratio of the first component to the second component is from 1/8 to 1/24 when the second component is citric acid; wherein the ratio of the first component to the second component is from 1/0.13 to 1/32 or from 1/80 to 1/600 when the second component is benzyl alcohol; and wherein the composition is substantially free of halogenated 3 isothiazolone.

10. A method of inhibiting the growth of microorganisms in a locus comprising introducing to, at or on, the locus a microorganism inhibiting amount of a synergistic mixture the first component of which is 2-methyl-3-isothiazolone, and the second component of which is one or more commercial microbicides selected from the group consisting of benzoic acid, sorbic acid, 1,2-dibromo-2,4-dicyanobutane, 1,3-dimethylol-5,5-dimethylhydantoin, phenoxyethanol, zinc pyrithione and climbazole; wherein a ratio of 2-methyl-3-isothiazolone to benzoic acid is from 1/0.13 to 1/8 or from 1/20 to 1/67, a ratio of 2-methyl-3-isothiazolone to sorbic acid is from 1/4 to 1/20, a ratio of 2-methyl-3-isothiazolone to 1,2-dibromo-2,4-dicyanobutane is from 1/10 to 1/20, a ratio of 2-methyl-3-isothiazolone to 1,3-dimethylol-5,5-dimethylhydantoin is from 1/11 to 1/20, a ratio of 2-methyl-3-isothiazolone to phenoxyethanol is from 1/30 to 1/80 or from 1/107 to 1/133, a ratio of 2-methyl-3-isothiazolone to zinc pyrithione is from 1/0.16 to 1/2.7, and a ratio of 2-methyl-3-isothiazolone to climbazole is from 1/0.6 to 1/1.3; and wherein the composition is substantially free of halogenated 3 isothiazolone; and wherein the amount of synergistic mixture is from 0.1 to 10,000 parts per million active ingredient.

11. The composition of claim 9 wherein the second component comprises citric acid and a ratio of 2-methyl-3-isothiazolone to citric acid is from 1/8 to 1/24.

12. The composition of claim 9 wherein the second component comprises benzyl alcohol and a ratio of 2-methyl-3-isothiazolone to benzyl alcohol is from 1/80 to 1/400.



13. The composition of claim 1 wherein the second component comprises phenoxyethanol and a ratio of 2-methyl-3-isothiazolone to phenoxyethanol is from 1/30 to 1/80.

14. The composition of claim 1 wherein the second component comprises benzoic acid and a ratio of 2-methyl-3-isothiazolone to benzoic acid is from 1/0.13 to 1/8 or from 1/20 to 1/67.

15. The composition of claim 1 wherein the second component comprises sorbic acid and a ratio of 2-methyl-3-isothiazolone to sorbic acid is from 1/4 to 1/20.

**(K) Evidence Appendix**

The Declarations of Eileen F. Warwick were submitted on January 23, 2009 and June 17, 2009. Copies of these documents are submitted herewith.

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**(L) Related Proceedings Appendix**

There are no related proceedings.

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